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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,404	03/16/2006	Ryuuichi Higuchi	TOYA108.013APC	8010

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EXAMINER	
BLAND, LAYLA D	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
02/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/572,404	HIGUCHI ET AL.	
	Examiner	Art Unit	
	LAYLA BLAND	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18 and 23* is/are pending in the application.

4a) Of the above claim(s) ____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 7, 2008 has been entered.

This Office Action is in response to Applicant's request for continued examination (RCE) filed November 7, 2008, declaration of Miyuki Tanaka, and amendment and response to the Final Office Action (mailed August 18, 2008), filed November 7, 2008 wherein claim 18 is amended, claims 1-17 and 19-22 are canceled, and claim 23 is newly submitted.

Claims 18 and 23 are pending and are examined on the merits herein.

In view of the cancellation of claims 1-17 and 19-22, all rejections made with respect to those claims in the previous office action are withdrawn.

In view of Applicant's amendment submitted November 7, 2008, the rejection of claim 18 under USC 102(b) as being anticipated by Yongchaiyudha is withdrawn. As shown in the declarations submitted November 7, 2008 and May 15, 2008, the aloe juice administered by Yongchaiyudha did not contain 0.001 to 10% by dry mass of the recited compounds.

The following are new rejections:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 23 is rejected under 35 U.S.C. 102(b) as being anticipated by Yongchaiyudha et al. (Phytomedicine Vol. 3 (3), pp. 241-243, 1996, PTO-1449 submitted May 22, 2006) as evidenced by Tanaka et al. (Biol. Pharm. Bull. 29(7) 1418-1422 (2006), of record).

Yongchaiyudha et al. teach that oral administration of one tablespoonful of *Aloe vera* juice twice a day in patients with diabetes resulted in lower blood sugar levels [see abstract]. Aloe gel also produced antihyperglycemic activity in rats which were given one tablespoon twice a day for at least a week [page 241, Introduction]. Various studies of administration of aloe gel up to 20g/kg showed no toxicity [page 241, second column, first paragraph]. For the preparation of *Aloe vera* juice, aloe juice was squeezed from aloe gel and combined with flavors, preservatives, and sweetening agent [page 242, Sample].

Tanaka et al. teach that the following compounds [page 1420, Figure 4] were isolated from Aloe vera gel [see abstract]:

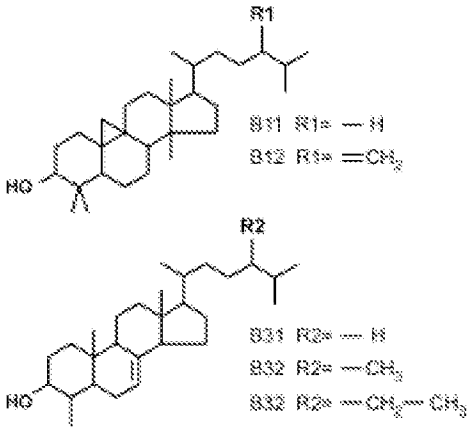


Fig. 4. Chemical Structures of Compounds B11, B12, B31, B32, and B33

Compound B11 is 9,19-cyclolanostan-3-ol and compound B12 is 24-methylene-9,19-cyclolanostan-3-ol. These compounds are inherently present in *Aloe vera* gel, which was administered to diabetic patients with the result of lower blood sugar levels. As noted by Applicant in the response dated November 7, 2008, aloe vera juice contains 9,19-cyclolanostan-3-ol and 24-methylene-9,19-cyclolanostan-3-ol in amounts of 222.8 ng and 162.3 ng, respectively. Given a dosage of 20g/kg, that is 0.004456 mg and 0.003246 mg of the recited compounds, respectively, which meets the limitation 0.001-50 mg/kg/day. Thus, claim 23 is anticipated.

Claims 18 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Ajabnoor (Journal of Ethnopharmacology, 28 (1990) 215-220, PTO-1449 submitted May 22, 2006), as evidenced by Tanaka et al. (Biol. Pharm. Bull. 29(7) 1418-1422 (2006), of record).

Ajabnoor teaches administration of an extract of *Aloe barbadensis* leaves and its bitter principle to alloxan-diabetic mice, resulting in a hypoglycemic effect [see abstract]. The extract was obtained by exhaustive liquid-liquid extraction with ethyl acetate and further purification by back extraction with saline and again with ethyl acetate [page 216, plant material]. The subjects were mice with induced hyperglycemia [page 216, Animals]. The mice were treated with up to 500mg/kg twice a day of aloe extract or 5 mg/kg of the bitter principle, resulting in decreased FPG [page 217, Results and Discussion].

Tanaka et al. teach that the following compounds [page 1420, Figure 4] were isolated from Aloe vera gel [see abstract]:

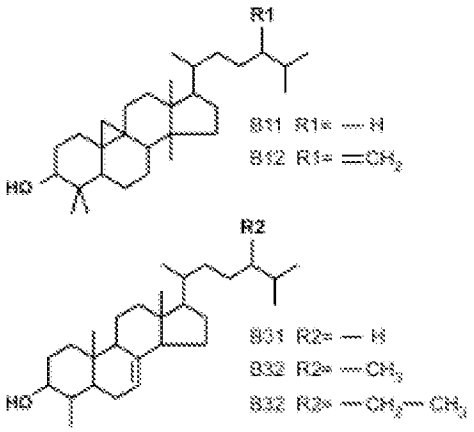


Fig. 4. Chemical Structures of Compounds B11, B12, B31, B32, and B33

Compound B11 is 9,19-cyclolanostan-3-ol and compound B12 is 24-methylene-9,19-cyclolanostan-3-ol. These compounds are inherently present in *Aloe vera* gel.

Ajabnoor does not teach the concentration or amount of 9,19-cyclolanostan-3-ol and 24-methylene-9,19-cyclolanostan-3-ol administered to the mice. However, it is expected that Ajabnoor's extract meets the claim limitations because Ajabnoor's extract was obtained in much the same way as is described in the instant specification: extraction of the plant material using a polar organic solvent. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

The following rejection is maintained and modified for relevancy to amended claim 18 and new claim 23:

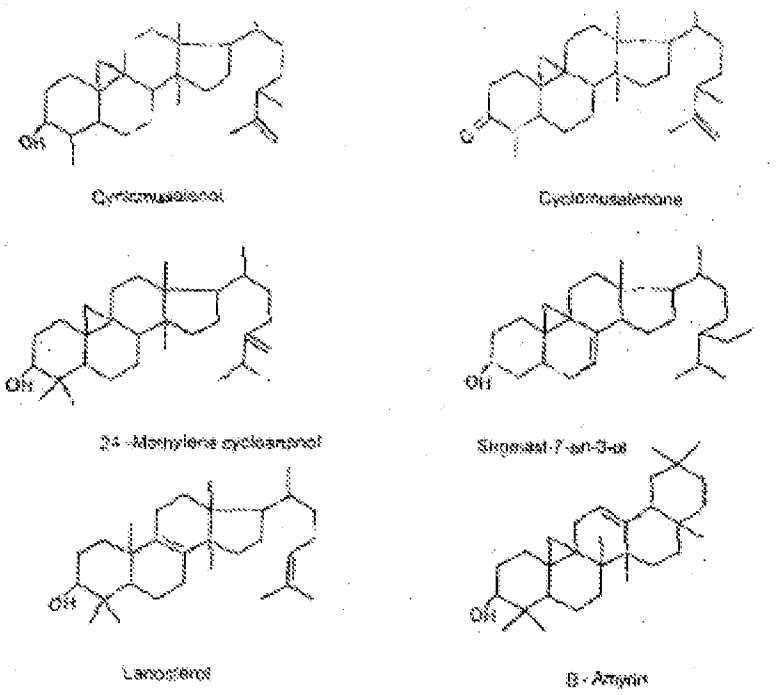
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18 and 23 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Abou Zeid (Egypt. J. Pharm. Sci. 39, No. 4-6, pp. 379-398 (1998), PTO-1449 submitted March 16, 2006).

Abou Zeid teaches that extracts of *M. cavendishii* and *M. sapientum* have hypoglycemic activity [page 379, third paragraph and page 393, Table 5]. The following compounds, including 24-methylene cycloartanol, [page 392, Figure] were isolated from the hexane extracts of *M. cavendishii* and *M. sapientum* leaves [page 387, second paragraph].



The hexane extract of the leaves was administered to diabetic rats [page 385, III and page 393, Table 5], resulting in at least 50% reduction in blood glucose after one week [page 393, Table 5].

Abou Zeid is silent regarding the amount and concentration of 24-methylene cycloartanol administered to the rats, and do not identify which of the above compounds is/are responsible for hypoglycemic activity. 24-methylene cycloartanol was isolated

from a hexane extract of the recited plants, however, so the concentration would be expected to be relatively high compared to administration of the whole plant. Furthermore, because 24-methylene cycloartanol is one of only 14 compounds exemplified and illustrated by Abou Zeid, it would have been obvious to try 24-methylene cycloartanol as a hypoglycemic agent.

The Supreme Court in KSR reaffirmed the familiar framework for determining obviousness as set forth in Graham v. John Deere Co. (383 U.S. 1, 148 USPQ 459 (1966)), but stated that the Federal Circuit had erred by applying the teaching-suggestion-motivation (TSM) test in an overly rigid and formalistic way. KSR, 82 USPQ2d 1385, 1396. Exemplary rationales that may support a conclusion of obviousness include “Obvious to try” – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success. MPEP 2143 states “a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely that product [was] not of innovation but of ordinary skill and common sense." In this case, it is clear that at the time of the invention, there was a recognized need for hypoglycemic drugs. Abou Zeid's hypoglycemic extract contained 8 flavonoids and 6 triterpenes [page 379, second paragraph], one of which was 24-methylenecycloartanol. This is a finite number of identified, predictable potential solutions to the recognized need for hypoglycemic drugs. One of ordinary skill in the art could have pursued the potential solutions, including 24-methylene cycloartanol with a reasonable expectation of success because Abou Zeid teaches one method for obtaining the compound by extraction, and the

compound was also previously known in the art [page 381, Authentic samples]. Thus, it would have been obvious to try 24-methylenecycloartanol for the treatment of hyperglycemia, and the skilled artisan could optimize the dosage using no more than routine experimentation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 18 and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 11/577,301. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of copending Application No. 11/577,301 are drawn to "a method for improving pancreatic functions"

using the same compounds as are claimed in the instant method of “improving hyperglycemia.” “Improving pancreatic functions” includes "improving hyperglycemia" within its scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/Layla Bland/
Examiner, Art Unit 1623